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- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations*
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(54) Title: METHOD FOR THE SELECTIVE AND QUANTITATIVE FUNCTIONALIZATION OF IMMUNOGLOBULIN FAB FRAGMENTS, CONJUGATE COMPOUNDS OBTAINED WITH THE SAME AND COMPOSITIONS THEREOF

(57) Abstract: The invention provides chemical conjugates between an immunoglobulin Fab fragment and molecular entities imparting diagnostic or therapeutic utility, whereby the only sites of conjugation on the Fab fragment are one or both of the sulfhydryl groups deriving from the selective and quantitative reduction of the inter-chain disulfide bond of said Fab fragment and whereby said molecular entities imparting diagnostic or therapeutic utility have at least one free sulfhydryl-reactive group, characterized in that the conjugation stoichiometric molar ratio molecular entity to Fab fragment is in the range from 0.95 to 1.05 or in the range from 1.95 to 2.05. The invention also provides a process for preparing said conjugates and pharmaceutical compositions thereof.



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A. CLASSIFICATION OF SUBJECT MATTER
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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ARTEAGA DE MURPHY C ET AL: "PHOSPHINE REDUCED IGG: A NEW METHOD FOR 99MTC LABELING IMMUNOGLOBULINS" JOURNAL OF RADIOANALYTICAL AND NUCLEAR CHEMISTRY, ARTICLES, ELSEVIER SEQUOIA S.A., LAUSANNE, CH, vol. 220, no. 1, 1997, pages 41-45, XP000199389 the whole document --- -/--	1-22

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>BURNS J A ET AL: "Selective reduction of disulfides by tris(2-carboxyethyl)phosphine" JOURNAL OF ORGANIC CHEMISTRY, AMERICAN CHEMICAL SOCIETY. EASTON, US, vol. 56, no. 8, 1991, pages 2648-2650, XP002149302 ISSN: 0022-3263 cited in the application Title Introduction part</p>	1-22
X	<p>SINGH RAJEEVA ET AL.: "Labeling of antibodies by in situ modification of thiol groups generated from selenol-catalyzed reduction of native disulfide bonds." ANALYTICAL BIOCHEMISTRY, vol. 304, - 2002 pages 147-156, XP001165655 Page 149, Paragraph "materials and methods", Biotinylation of antibody by selenol/TCEP reduction of native disulfide bonds to thiol groups... Paragraph "results", "discussion" page 148, left-hand column, paragraph 2; figure 1</p>	1-22
Y	<p>ANELLI ET AL: "L-Glutamic acid and L-lysine as useful building blocks for the preparation of bifunctional DTPA-like ligands" BIOCONJUGATE CHEMISTRY, vol. 10, no. 1, 1999, pages 137-140, ABSTRACT, XP002115959 cited in the application XP002148891 the whole document</p>	1-22
X	<p>SEITZ U ET AL: "PREPARATION AND EVALUATION OF THE RHENIUM-188-LABELLED ANTI-NCA ANTIGEN MONOCLONAL ANTIBODY BW 250/183 FOR RADIOIMMUNOTHERAPY OF LEUKAEMIA" EUROPEAN JOURNAL OF NUCLEAR MEDICINE, BERLIN, DE, vol. 26, no. 10, October 1999 (1999-10), pages 1265-1273, XP000952569 ISSN: 0340-6997 cited in the application Paragraph "materials and methods", Radiolabelling of antibody with 188Re. Paragraph Results, reduction of antibody and labelling with 188Re Discussion part</p>	1-22

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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